

EXTRADURAL DIAMORPHINE WITH ADRENALINE IN LABOUR: COMPARISON WITH DIAMORPHINE AND BUPIVACAINE

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SUMMARY

In a randomized double-blind study of 51 primigravida, we have examined the relative efficacies of bupivacaine, diamorphine or diamorphine with adrenaline given by the extradural route for relief of pain during labour. Group 1 (n = 18) received diamorphine 5 mg in 0.9% sodium chloride 8 ml; group 2 (n = 19) received diamorphine 5 mg in 0.9% sodium chloride 8 ml with 1:200 000 adrenaline; group 3 (n = 14) received 0.375% bupivacaine 8 ml. All patients received 0.375% bupivacaine 8 ml as a supplement after the initial analgesia had subsided. Patients in all groups had satisfactory and comparable analgesia 20 min after the initial injection. However, after 60 min and up to 8 h, analgesia was superior in group 2 as assessed by linear analogue pain scores, with statistical significance at 4, 6 and 8 h. Groups 1 and 2 required bupivacaine supplements less frequently than group 3 (P < 0.001). There were no serious adverse effects in any group, but pruritus was a feature in the diamorphine groups. Diamorphine 5 mg may be used as an alternative to bupivacaine 0.375% 8 ml in the first stage of labour and provides a longer duration of action. The addition of adrenaline 1:200 000 appears to augment both the quality and duration of analgesia.

KEY WORDS

Anaesthesia: obstetric. Analgesics: diamorphine, extradural. Anaesthetics, local: bupivacaine.

Local anaesthetic agents have achieved widespread acceptance as extradural analgesics in labour, but at the expense of adverse effects, such as hypotension, bradycardia, paraesthesia, motor

block and urinary retention. The risk of intravascular injection, more likely in the presence of the extradural venous engorgement of labour, and the possibility of inadvertent intrathecal injection have stimulated research into alternative analgesic techniques.

It has been shown that extradural diamorphine 5 mg, when combined with bupivacaine, provides superior analgesia with fewer bupivacaine supplements in primigravidae in labour [1]. The addition of a vasoconstrictor, such as adrenaline 1:200 000, is used commonly to decrease systemic uptake of local anaesthetics from the extradural space. A greater duration of analgesia following Caesarean section was found when adrenaline was added to diamorphine compared with diamorphine in saline [2], both given extradurally.

This study was designed to examine the efficacy of diamorphine as a sole extradural analgesic compared with bupivacaine, and to assess if the addition of adrenaline to diamorphine would be advantageous.

PATIENTS AND METHODS

In a randomized, double-blind trial, we studied 51 primigravid women (ASA I-II) who requested extradural analgesia in labour. Informed consent was obtained and the study was approved by the hospital Ethics Committee. No patient had received opioid analgesia by any route on the day of study.

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TABLE I. Patient characteristics (mean (SEM or range))

	Group 1	Group 2	Group 3
Age (yr)	22.25 (17-28)	23.7 (17-32)	24.3 (20-31)
Weight (kg)	78.3 (2.95)	77 (2.94)	75 (3.1)
Duration of labour after extradural (min)	505 (45)	571 (56.4)	449 (56.1)

The drugs were pre-packaged in numbered envelopes and randomized by the hospital pharmacy department using random number tables. Patients received an i.v. preload of compound sodium lactate solution 500 ml before insertion of 3 cm of catheter in either the L2-3 or L3-4 extradural space.

Three groups were studied. Group 1 patients ($n = 18$) received diamorphine 5 mg in 0.9% sodium chloride 8 ml. Group 2 ($n = 19$) received diamorphine 5 mg in 0.9% sodium chloride 8 ml with 1:200 000 adrenaline. The adrenaline solution contained also sodium metabisulphite as an antioxidant. Group 3 received 0.375% bupivacaine 8 ml. Supplements of 0.375% bupivacaine 8 ml were given to all patients when analgesia subsided, prior assurance having been given that an effective drug was available if the trial drug was ineffective.

The diamorphine was prepared in the relevant solvent to an 8-ml volume by either an anaesthetic colleague or a senior midwife. The 0.375% bupivacaine was drawn up from a prepared ampoule. The unlabelled syringe was given to the operator.

Initially, the study had been designed to contain 60 patients, 20 in each group. Six women had incomplete records and were unassessable. Three envelopes contained broken ampoules and were discarded.

The attending midwife documented all data except for analgesia. Heart rate and systemic arterial pressure were measured every 5 min for 30 min after each bolus of extradural drug.

Analgesia, sedation, ventilatory frequency, heart rate, arterial pressure and adverse effects such as paraesthesiae, pruritus, urinary retention, motor block, nausea and vomiting were noted. Assessments were made at 0 min (before drug administration) and at 20, 40 and 60 min and 2, 4, 6, 8 and 12 h.

Analgesia was evaluated using a linear analogue scale [3]. On a 10-cm line (one end representing "no pain at all", the other the "worst pain

imaginable") patients were asked to mark where they assessed the severity of their pain. Sedation was measured using a four-point sedation scale: 0 = wide awake; 1 = drowsy; 2 = very drowsy; 3 = sleeping. The times taken to require bupivacaine supplements were noted. Fetal state was assessed using the Apgar scoring system.

Results were analysed statistically using one-way analysis of variance, chi-square tests, Yates' correlation, the Logrank test and the F test where suitable.

RESULTS

There were no significant differences between the groups in age, weight and duration of labour under extradural analgesia (table I).

Satisfactory analgesia with comparable pain scores was achieved in all three groups after 20 min. Between 60 min and 8 h, analgesia was superior in group 2, being significant at 4, 6 and 8 h ($P = 0.006$, $P = 0.03$ and $P = 0.04$, respectively) (fig. 1). There were no significant differences between groups 1 and 3.

In groups 1 and 2, there was a significantly longer time to the first bupivacaine supplement ($P < 0.001$) compared with group 3. There was a small but non-significant difference between groups 1 and 2 in this respect (table II).

The mean interval between supplements was significantly less in group 3 compared with groups 1 and 2 (table II) ($P < 0.001$). However, there was no difference between groups 1 and 2.

There was a tendency for both opioid groups to require bupivacaine supplements later than the bupivacaine group, and for group 2 (diamorphine with adrenaline) to require supplements last (fig. 2).

Sedation was greater in the opioid groups, but this was significant only at 20 and 40 min. Peak sedation times occurred at 20 min in the diamorphine group, and at 4 h in the diamorphine with adrenaline group (table III).

Mild hypotension occurred in three group 1 patients and one group 3 patient, in whom systolic

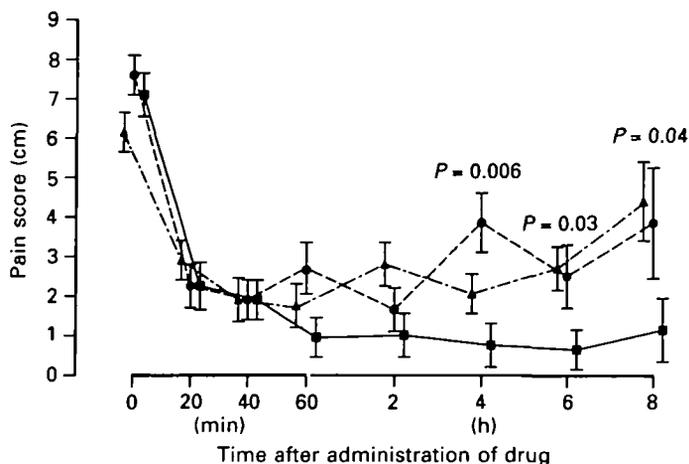


FIG. 1. Linear analogue pain scores (mean, SEM) in groups 1 (▲), 2 (■) and 3 (●).

TABLE II. Bupivacaine supplements (mean (SEM)). $P < 0.001$ for the differences between group 3 and groups 1 and 2 by Logrank analysis

	Time to first supplement (min)	Interval between supplements (min)
Group 1	135 (23.3)	163 (9.2)
Group 2	171 (22.7)	163 (8.9)
Group 3	99 (26.5)	106 (10.4)

TABLE III. Sedation scores (mean (SEM))

Time	Group 1	Group 2	Group 3	P
20 min	1 (0.18)	0.68 (0.15)	0.08 (0.07)	< 0.01
40 min	0.95 (0.15)	0.84 (0.12)	0.08 (0.07)	< 0.001
60 min	0.75 (0.22)	0.67 (0.13)	0.22 (0.11)	
2 h	0.8 (0.18)	0.83 (0.19)	0.23 (0.12)	
4 h	0.71 (0.19)	1.2 (0.31)	0.7 (0.39)	

arterial pressures of < 100 mm Hg were recorded. No patient required a vasoconstrictor and the differences were statistically insignificant. No patient developed a ventilatory frequency less than 10 b.p.m. at any time.

Eight patients in group 1 ($n = 18$), nine in group 2 ($n = 19$) and seven in group 3 ($n = 14$) developed nausea or vomiting. Using the chi-square test, no significant differences were found between the groups. Nine patients in group 1, 10 in group 2 and six in group 3 developed urinary retention. Again, the chi-square test showed no

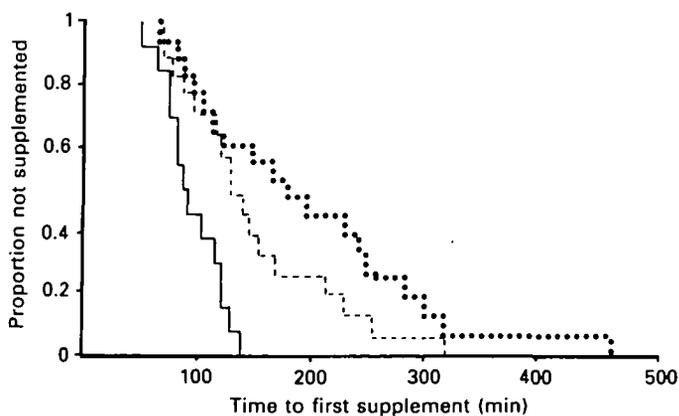


FIG. 2. Cumulative survival curve of time to first supplement of bupivacaine in groups 1 (---), 2 (●●●) and 3 (—).

difference between the groups. Nausea, vomiting and urinary retention increased with progress of labour.

Paraesthesiae were minimal in the opioid groups during the first 2 h, but increased as more bupivacaine supplements were given. However, 4 h after the initial injection, significantly fewer group 2 patients had paraesthesiae ($P = 0.001$).

Pruritus was absent in the bupivacaine group, 12 of group 1 and 14 of group 2 patients experienced this side effect ($P = 0.05$, $P = 0.005$ and $P = 0.01$ at 60 min, 2 and 4 h, respectively).

Motor block was initially less in the opioid groups, but increased as more bupivacaine was given. No statistical differences were obtained.

Apgar scores were generally satisfactory. However, one baby in group 1 had Apgar scores of 3 and 8 at 2 and 5 min, respectively. Another in group 3 had scores of 4 and 10 at the same times. Both had undergone delivery by forceps.

DISCUSSION

Pethidine was an early opioid to be given extradurally [4] and it was shown to be effective in labour to a varying degree. Its short duration of action led Perris and Malins to add adrenaline 1:200 000 in a subsequent study [5] and this produced a longer duration of action. Other work [6] compared pethidine and saline with pethidine and adrenaline, and failed to detect any significant differences in either efficacy or duration of action. Husemeyer and colleagues [7] suggested that extradural pethidine compared favourably with i.m. pethidine because of greater plasma concentrations, rather than a specific spinal cord action. However, Vella and others [8] demonstrated that fentanyl has a potent extradural effect in labour, supporting earlier work [9] which showed distinct superiority of extradural over i.m. fentanyl for obstetric analgesia. Extradural pethidine [5], fentanyl [10], alfentanil [11] and morphine [12] appear to provide poor analgesia in the second stage. Analgesia during the first stage was found by Heytens to be good with alfentanil [11], but some neonates in this study were hypotonic.

Extradural morphine has been shown to be of variable efficacy in low doses [13–15] for obstetric analgesia, but Hughes and colleagues [12] obtained greater reliability with doses of 7.5 mg, although they suggested a local anaesthetic given extradurally would be more suitable for the second stage.

Later studies have used local anaesthetic–opioid mixtures in order to reduce the doses of both types of drug. Thus fentanyl–bupivacaine mixtures [16] in low concentration extradural infusions produced good analgesia with reduced motor block, whilst sufentanil with bupivacaine and adrenaline decreased onset time whilst increasing quality and duration of analgesia compared with bupivacaine alone [17].

In this study we have compared extradural diamorphine with bupivacaine. We have also examined the effect of adrenaline 1:200 000 on the efficacy and duration of action of diamorphine. In these respects, our study differed considerably from that of McGrady, Brownhill and Davis [1] who showed that a combination of diamorphine and bupivacaine by infusion was highly effective.

We observed that diamorphine 5 mg and 0.375% bupivacaine 8 ml were comparable in terms of analgesia. Both had a rapid onset time and most patients obtained satisfactory pain scores after 20 min. Extradural diamorphine enters the spinal cord rapidly, as it is lipophilic. It may pass through the dura, through the arachnoid granulations or via the posterior radicular arteries to the cord [18]. Diamorphine thus has a more rapid and predictable onset time than morphine which, although it is a smaller molecule and crosses the dura faster [19], is more hydrophilic.

Adrenaline reduces the vascular uptake of diamorphine from tissues, and this may account for the superior analgesia in group 2 from 60 min to the end of the study.

Despite the recommendations of *Martindale: the Extra Pharmacopoeia* [20], diamorphine was dissolved in saline to improve the tonicity of our solutions. Studies by Hain and Kirk [21] have suggested that this concentration (0.0625%) would be unlikely to precipitate even 24 h after constitution. In our study, solutions were used immediately after preparation and no precipitates were observed.

Sedation was greater in both opioid groups. It is interesting that peak sedation scores occurred later in group 2 (the adrenaline group) than in group 1. There was no case of oversedation and neonatal Apgar scores did not differ between groups. In addition, respiratory depression was not observed. Patients were monitored throughout labour and post partum observations did not reveal a ventilatory frequency less than 10 b.p.m. However, ventilatory frequency may not be a satisfactory index of hypoventilation [22].

In conclusion, we have observed that extradural diamorphine produced comparable analgesia of longer duration than bupivacaine in the doses used. The addition of adrenaline improved longer term analgesia and duration of action with fewer paraesthesiae and reduced requirements for bupivacaine supplements.

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